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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/033,167	12/27/2001	David Botstein	P2930R1C10	7373

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EXAMINER	
FREDMAN, JEFFREY NORMAN	

ART UNIT	PAPER NUMBER
1637	

DATE MAILED: 03/16/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/033,167	BOTSTEIN ET AL.	
	Examiner	Art Unit	
	Jeffrey Fredman	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 January 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *27,28,32-34 and 42-46* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *42-46* is/are allowed.

6)☒ Claim(s) *27-28, 32-34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on January 31, 2005 has been entered.

Claim Rejections - 35 USC § 112 – Written Description

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 27-28 and 32-34 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

In analysis of the claims for compliance with the written description requirement of 35 U.S.C. 112, first paragraph, the written description guidelines note regarding genus/species situations that "Satisfactory disclosure of a ``representative number'' depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed." (See: Federal Register:

December 21, 1999 (Volume 64, Number 244), revised guidelines for written description.)

All of the current claims encompass a genus of nucleic acids which are different from those disclosed in the specification due to the use of the "hybridization" language. The use of the "hybridization" language causes the claims to include variants for which no written description is provided in the specification since there is no description of any other sequences besides SEQ ID NO: 6 which "hybridize" to SEQ ID NO: 6. The specification has express possession of only one sequence, SEQ ID NO: 6, in a genus which comprises hundreds of trillions of different possibilities.

A central element in the utility guidelines and in the caselaw is whether there is substantial variation among the species in the broader genus which would share the inventive features of the disclosed sequence. Here, no common element or attributes of the sequences are disclosed, not even the presence of certain domains. No structural limitations or requirements which provide guidance on the identification of sequences which meet these functional limitations is provided. Further, these claims encompass alternately spliced versions of the proteins, allelic variants including insertions and mutations, inactive precursor proteins which have a removable amino terminal end, and only specific amino acid sequences have been provided. No written description of alleles, of upstream or downstream regions containing additional sequence, or of alternative splice variants has been provided in the specification.

So while Example 9 of the utility guidelines reads stringent hybridization conditions as yielding less variation, the variation in the current case is significant

because there is no expectation that other sequences which hybridize to SEQ ID NO: 6 would themselves hybridize to targets which are overexpressed in cancer cells, which is the asserted utility of SEQ ID NO: 6. One central problem with the current claims is that the while such variants of SEQ ID NO: 6 are likely to exist, there is a complete absence of knowledge on the part of applicant as to what sequence comprises these variants.

It is noted in the recently decided case The Regents of the University of California v. Eli Lilly and Co. 43 USPQ2d 1398 (Fed. Cir. 1997) decision by the CAFC that

> "A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is. See Fiers, 984 F.2d at 1169- 71, 25 USPQ2d at 1605- 06 (discussing Amgen). It is only a definition of a useful result rather than a definition of what achieves that result. Many such genes may achieve that result. The description requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See In re Wilder, 736 F.2d 1516, 1521, 222 USPQ 369, 372- 73 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate."). Accordingly, naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material. "

In the current situation, the definition of the claimed sequences using the "hybridization" language lacks any specific required structure. This is precisely the situation of naming a type of material which is generally known to likely exist, but, except for SEQ ID NO: 6 itself, is in the absence of knowledge of the material composition and fails to provide descriptive support for the generic claim to anything which hybridizes to SEQ ID NO: 6 under stringent conditions.

It is noted that in Fiers v. Sugano (25 USPQ2d, 1601), the Fed. Cir. concluded that

> "...if inventor is unable to envision detailed chemical structure of DNA sequence coding for specific protein, as well as method of obtaining it, then conception is not achieved until reduction to practice has occurred, that is, until after gene has been isolated...conception of any chemical substance, requires definition of that substance other than by its functional utility."

In the instant application, certain specific SEQ ID NOs are described. Also, in Vas-Cath Inc. v. Mahurkar (19 USPQ2d 1111, CAFC 1991), it was concluded that:

> "...applicant must also convey, with reasonable clarity to those skilled in art, that applicant, as of filing date sought, was in possession of invention, with invention being, for purposes of "written description" inquiry, whatever is presently claimed."

In the application at the time of filing, there is no record or description which would demonstrate conception of any nucleic acids other than SEQ ID NO: 6. There is no conception of sequences which "hybridize" to SEQ ID NO: 6 except by the functional utility of "hybridization." Applicant has no definition of the structure of these molecules or of any structural element relating to these molecules whatsoever. The entire claim is functionally drawn to claim compounds which Applicant does not have, which Applicant has not made and which comprise specific sequences that Applicant does not know. These claims therefore fail to meet the written description requirement by encompassing sequences which are not described in the specification.

Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

5. Claims 27, 28 and 32-34 are rejected under 35 U.S.C. 102(a) as being anticipated by Genbank Accession No. AC004089 (30 January 1998).

Genbank Accession No. AC004089 teaches a sequence which comprises a 22 nucleotide sequence with 100% identity to nucleotides 289-310 of SEQ ID NO: 6.

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Score = 44.1 bits (22), Expect = 0.32
 Identities = 22/22 (100%)
 Strand = Plus / Plus


Query: 289    agaagcggcgcctggaggcaga 310
              ||||||||||||||||||||||
Sbjct: 101898 agaagcggcgcctggaggcaga 101919
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The calculated Tm of these 22 nucleotides is minimally 62 degrees C as calculated by the Oligonucleotide properties calculator (see http://www.basic.nwu.edu/biotools/oligocalc.html). Consequently, this sequence would hybridize under the required conditions and anticipates claims 27, 28 and 32-34. With regard to the functional requirement, this sequence would inherently meet that requirement since it necessarily must hybridize to its complement.

Allowable Subject Matter

6. Claims 42-46 are allowed.

7. The following is a statement of reasons for the indication of allowable subject matter: Claims 42-46 are drawn to the specific SEQ ID NO:6 or encoding SEQ ID NO: 7 sequences and there is no prior art that suggest these sequences and they are fully described because the claims do not permit the variation permitted by the hybridization language.

Response to Arguments

8. Applicant's arguments filed January 31, 2005 have been fully considered but they are not persuasive.

All of the arguments made in the previous final rejection are maintained and continue to apply.

The amendment to include a function of "two fold overexpression" for the nucleic acid does not affect the rejection because this function imposes no structural limitation on the nucleic acids themselves. That is, unlike the guideline situation of example 9 where the function of the protein requires conservation of enzymatic activity and consequent conservation of a significant sequence which would encode the amino acids necessary to achieve that function, the function of "two fold overexpression" requires no significant conservation at all. Any nucleic acid sequence of sufficient length to hybridize would meet the claim, with a Tm of about 55 C. The addition of a function does not reduce or address the size of this genus.

With regard to the arguments on Lilly and Fiers, this is the precise type of situation that the Federal Circuit appeared to be attempting to avoid. The Federal Circuit voided the grant of patents where single species were used to claim an entire

genus of molecules for which the patentee lacked any descriptive characteristics other than functional. The same situation obtains here and the precedent of the Federal Circuit leads to the same result.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey Fredman whose telephone number is (571)272-0742. The examiner can normally be reached on 6:30-3:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571)272-0782. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Jeffrey Fredman
Primary Examiner
Art Unit 1637
3/10/05